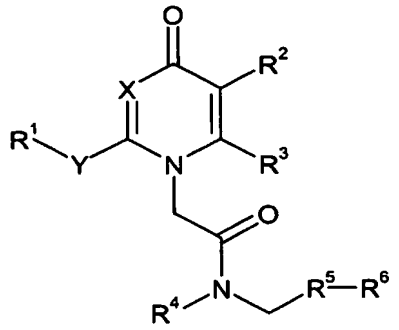
Claims

1. A compound of formula (I) :



(I)

in which:

R^1 is an aryl group, optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from $C_{(1-6)}$alkyl, $C_{(1-6)}$alkoxy, $C_{(1-6)}$alkylthio, aryl$C_{(1-6)}$alkoxy, hydroxy, halogen, CN, COR^7, carboxy, $COOR^7$, NR^7COR^8, $CONR^9R^{10}$, $SO_2NR^9R^{10}$, $NR^7SO_2R^8$, NR^9R^{10}, mono to perfluoro-$C_{(1-4)}$alkyl, mono to perfluoro-$C_{(1-4)}$alkoxyaryl, and aryl$C_{(1-4)}$alkyl;

R^2 is halogen, $C_{(1-3)}$alkyl, $C_{(1-3)}$alkoxy, hydroxy$C_{(1-3)}$alkyl, $C_{(1-3)}$alkylthio, $C_{(1-3)}$alkylsulphinyl, amino$C_{(1-3)}$alkyl, mono- or di-$C_{(1-3)}$alkylamino$C_{(1-3)}$alkyl, $C_{(1-3)}$alkylcarbonylamino$C_{(1-3)}$alkyl, $C_{(1-3)}$alkoxy$C_{(1-3)}$alkylcarbonylamino$C_{(1-3)}$alkyl, $C_{(1-3)}$alkylsulphonylamino$C_{(1-3)}$alkyl, $C_{(1-3)}$alkylcarboxy, $C_{(1-3)}$alkylcarboxy$C_{(1-3)}$alkyl, and

R^3 is hydrogen, halogen, $C_{(1-3)}$alkyl, or hydroxy$C_{(1-3)}$alkyl; or

R^2 and R^3 together with the pyridone or pyrimidone ring carbon atoms to which they are attached form a fused 5-or 6-membered carbocyclic ring; or

R^2 and R^3 together with the pyridone or pyrimidone ring carbon atoms to which they are attached form a fused benzo or heteroaryl ring optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from halogen, $C_{(1-4)}$alkyl, cyano, $C_{(1-3)}$alkoxy$C_{(1-3)}$alkyl, $C_{(1-4)}$alkoxy or $C_{(1-4)}$alkylthio, or mono to perfluoro-$C_{(1-4)}$alkyl;

R^4 is Het-$C_{(0-4)}$alkyl in which Het is a 5- to 7- membered saturated heterocyclyl ring comprising N and optionally O or S, and in which N is substituted by C_{3-8}cycloalkyl or $C_{(1-6)}$alkyl further substituted by 1, 2 or 3 substituents selected from R^{11}, $COOR^{11}$, $COOCH_2R^{11}$, COR^{11}, CN, $CONR^{12}R^{13}$, C_{3-8}cycloalkyl, vinyl optionally substituted by halogen or $C_{(1-3)}$alkyl and a 5- to 7-membered saturated heterocyclyl ring comprising N in which N may be substituted by C_{1-3}alkyl;

R^5 is an aryl or a heteroaryl ring optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from $C_{(1-6)}$alkyl, $C_{(1-6)}$alkoxy, $C_{(1-6)}$alkylthio, aryl$C_{(1-6)}$alkoxy, hydroxy, halogen, CN, COR^7, carboxy, $COOR^7$, NR^7COR^8, $CONR^9R^{10}$, $SO_2NR^9R^{10}$, $NR^7SO_2R^8$, NR^9R^{10}, mono to perfluoro-$C_{(1-4)}$alkyl and mono to perfluoro-$C_{(1-4)}$alkoxy;

R^6 is an aryl or a heteroaryl ring which is further optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from $C_{(1-6)}$alkyl, $C_{(1-6)}$alkoxy, $C_{(1-6)}$alkylthio, $C_{(1-6)}$alkylsulfonyl, aryl$C_{(1-6)}$alkoxy, hydroxy, halogen, CN, COR^7, carboxy, $COOR^7$, $CONR^9R^{10}$, NR^7COR^8, $SO_2NR^9R^{10}$, $NR^7SO_2R^8$, NR^9R^{10}, mono to perfluoro-$C_{(1-4)}$alkyl and mono to perfluoro-$C_{(1-4)}$alkoxy, or $C_{(5-10)}$alkyl;

R^7 and R^8 are independently hydrogen or $C_{(1-12)}$alkyl, for instance $C_{(1-4)}$alkyl (e.g. methyl or ethyl);

R^9 and R^{10} which may be the same or different is each selected from hydrogen, or $C_{(1-12)}$alkyl, or R^9 and R^{10} together with the nitrogen to which they are attached form a 5- to 7 membered ring optionally containing one or more further heteroatoms selected from oxygen, nitrogen and sulphur, and optionally substituted by one or two substituents selected from hydroxy, oxo, $C_{(1-4)}$alkyl, $C_{(1-4)}$alkylcarboxy, aryl, e.g. phenyl, or aralkyl, e.g benzyl, for instance morpholine or piperazine;

R^{11} is an unsubstituted 5- or 6-membered heteroaryl or an unsubstituted 6-membered aryl, or a 5- or 6-membered heteroaryl or a 6-membered aryl substituted by one or more R^{14}.

R^{12} is selected from hydrogen or C_{1-3}alkyl;

R^{13} is selected from phenyl optionally substituted by halogen, C_{1-6}alkyl, C_{1-6}alkoxy or cyano, or C_{5-7}cycloalkyl;

R^{14} is selected from the group consisting of halogen, CF_3, C_{1-6}alkyl, C_{1-6}alkoxy or cyano;

X is CH or nitrogen; and

Y is a $C_{(2-4)}$alkylene group (optionally substituted by 1, 2 or 3 substituents selected from methyl and ethyl), CH=CH, or $(CH_2)_nS$ where n is 1, 2 or 3,

and a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 wherein R^1 is phenyl optionally substituted by 1, 2, 3 or 4 halogen substituents.

3. A compound according to claim 2 wherein R^1 is phenyl substituted by 1 to 3 fluoro.

4. A compound according to any of claims 1 to 3 wherein X is CH and R^2 and R^3 together with the pyridone ring carbon atoms to which they are attached form a fused benzo or pyrido ring optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from halogen, $C_{(1-4)}$alkyl, cyano, $C_{(1-3)}$alkoxy$C_{(1-3)}$alkyl, $C_{(1-4)}$alkoxy or $C_{(1-4)}$alkylthio, or mono to perfluoro-$C_{(1-4)}$alkyl.

5. A compound according to claim 4 wherein the fused benzo or pyrido ring is unsubstituted.

6. A compound according to any of claims 1 to 3 wherein X is nitrogen and R^2 and R^3 together with the pyrimidone ring carbon atoms to which they are attached form a fused 5-membered carbocyclic (cyclopentenyl) or benzo ring optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from halogen, $C_{(1-4)}$alkyl, cyano, $C_{(1-3)}$alkoxy$C_{(1-3)}$alkyl, $C_{(1-4)}$alkoxy, $C_{(1-4)}$alkylthio, or mono to perfluoro-$C_{(1-4)}$alkyl.

7. A compound according to claim 6 wherein the fused 5-membered carbocyclic or benzo ring is unsubstituted.

8. A compound according to any of claims 1 to 7 wherein R^4 is Het $C_{(0)}$alkyl in which Het is a six-membered saturated heterocyclyl ring comprising nitrogen in which the nitrogen is substituted by C_{3-8}cycloalkyl or $C_{(1-2)}$alkyl substituted by a single substituent selected from R^{11}, $COOR^{11}$, $COOCH_2R^{11}$, COR^{11}, CN, $CONR^{12}R^{13}$, C_{3-8}cycloalkyl, vinyl optionally substituted by halogen or methyl and a 5- or 6- membered saturated heterocyclyl ring comprising N in which the nitrogen may be substituted by methyl.

9. A compound according to any of claims 1 to 8 wherein R^5 is phenyl and R^6 is phenyl substituted by mono to perfluoro-$C_{(1-4)}$alkyl, halogen or $C_{(1-6)}$alkyl.

10. A compound according to claim 9 wherein R^6 is phenyl substituted by trifluoromethyl.

11. A compound to any of claims 1 to 10 wherein Y is CH_2S.

12. A compound as named in any of Examples 1 to 29.

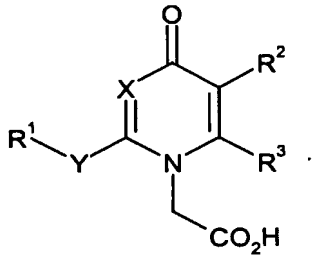
13. A pharmaceutical composition comprising a compound of formula (I) according to any of claims 1 to 12 and a pharmaceutically acceptable carrier, optionally with one or more other therapeutic compounds.

14. A compound of formula (I) according to any of claims 1 to 12 for use in therapy.

15. The use of a compound of formula (I) according to any of claims 1 to 12 for the manufacture of a medicament for treating atherosclerosis.

16. A method of treating a disease associated with activity of the enzyme Lp-PLA_2 which method involves treating a patient in need thereof with a therapeutically effective amount of a compound of formula (I) according to any of claims 1 to 12.

17. A process for preparing a compound of formula (I) which process comprises reacting an acid compound of formula (II):



(II)

in which X, Y, R^1, R^2 and R^3 are as hereinbefore defined,
with an amine compound of formula (III):

$$R^6\text{-}R^5\text{-}CH_2NHR^4 \quad \text{(III)}$$

in which R^4, R^5 and R^6 are as hereinbefore defined; under amide forming conditions.